

***Remarks***

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 64 through 90 are pending in the application, with 64 and 71 being the independent claims. Claims 65-66, 75-82, and 88-90 have been indicated as withdrawn from consideration. Claims 64 and 71 are amended to add the phrase "forming a lipid complex by" after the "(a)." The word "compound" has been stricken from Claim 74 and replaced with a word "method." These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Requirement for Restriction/Election***

Applicant thanks the Examiner for removing the restriction requirement with respect to Groups I and II. Accordingly, the Examiner stated that "[t]he claims corresponding to the elected subject matter are claims 64, 67-74, and 83-87 and such claims are herein acted on the merits." *See* Office Action at 3.

***Expansion of Election of Species Requirement***

Applicant thanks the Examiner for acknowledging that "the prior art at the time of the invention was such that it did not anticipate or render obvious the elected species of DMRIE carboxylate propyl amide for use in a method of delivering an anionic molecule into a cell." *See* Office Action at 3. Applicant acknowledges the Examiner's expansion of search and examination to cover the compounds of the formula presented in claim 64.

***Objection to the Claims (New Grounds of Objection)***

The Examiner pointed out a discrepancy in the preamble for claim 74. Claim 74 has been amended herein to correct the discrepancy by replacing "compound" with "method." Reconsideration and withdrawal of the rejection is respectfully requested.

***Claim Rejection - 35 USC § 112, Second Paragraph (New Grounds of Rejection)***

The Office has rejected claims 64, 67-74, and 83-87 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Particularly, the Examiner stated that there is "insufficient antecedent basis for the limitation "the lipid complex" in each of claims 64 and 71, since the preceding text of claims 64 or 71 fail to set forth any reference to "a lipid complex" *per se*". Each of the claims 64 and 71 are amended herein to make explicit the formation of a "lipid complex." Reconsideration and withdrawal of the rejection is respectfully requested.

***Claim Rejections - 35 USC § 103 (New Grounds of Rejection)***

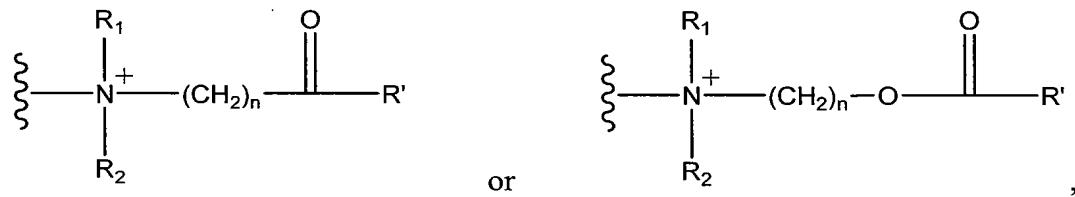
The Office has rejected claims 64, 67, 69-70, and 83-84 under 35 U.S.C. § 103(a) as being obvious over Nantz *et al.* (U.S. Patent No. 5,869,715) in view of Felgner (WO 91/17424). Applicant respectfully traverses.

To make a *prima facie* case of obviousness under Section 103(a), the Office must establish that each and every claim limitation is taught or suggested in the reference. M.P.E.P. § 2143.03. Nantz in view of Felgner do not teach or suggest every feature of claims 64, 67, 69-70, and 83-84.

The Office contends that the Nantz disclosure teaches cationic lipid compounds having a lipophilic region similar to that of the present invention, and a hydrophilic

region. The Office further notes that, similarly to the presently claimed invention, the hydrophilic region of the compounds disclosed by Nantz contains a positively charged quaternary nitrogen. The Examiner concludes that lipid compounds disclosed by Nantz correspond to compounds defined by Applicant's claims.

The nitrogen in the Nantz compounds is substituted with, *inter alia*, acyl or acyloxy containing alkyl group. Consequently, the hydrophilic region of the compounds disclosed in Nantz appears to have, *inter alia*, the following general chemical formulas:

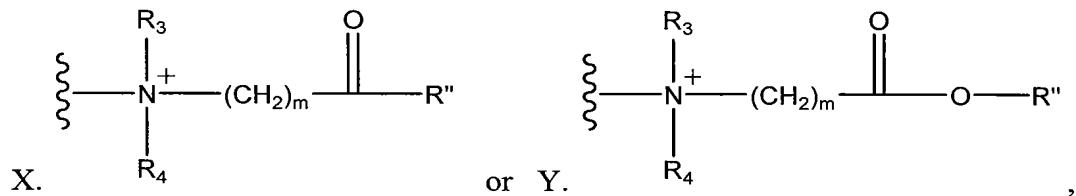


wherein n is 1-10, and R<sub>1</sub>, R<sub>2</sub> and R' are alkyl groups. *See* Nantz at col. 3, ll. 42-67. As disclosed in Nantz, the three preferred compounds of the invention are cytofectins wherein nitrogen is substituted with a hydroxylated alkyl (Compound A, col. 4, ll. 23-30), an ether containing alkyl (Compound B, col. 5, ll. 42-50), and a halogenated alkyl (Compound C, col. 7, ll. 10-20). The preference for the above compounds is further provided by the disclosures of generalized synthetic schemes for these compounds (col. 4-col. 13).

Nantz's disclosure appears to be inconsistent in reciting the embodiments of the invention. The abstract and the summary of the invention fail to disclose cytofectins wherein a quaternary nitrogen is substituted with acyl or acyloxy containing alkyl group (face of the patent, col. 2, ll. 60-64, and col. 3, ll. 15-20). Nor does Nantz teach or suggest a method of making or using such compounds. In fact, based on the organization and the language of Nantz disclosure, a person skilled in the art would be taught away

from making cytofectins containing quaternary nitrogen substituted with acyl or acyloxy containing alkyl group.

The hydrophilic region of compounds previously claimed in claims 64, 67, 69-70, and 83-84 of the captioned application could have, *inter alia*, the following general chemical formulae X and Y:



wherein m is 1-10, and R<sub>3</sub>, R<sub>4</sub> and R'' are alkyl groups.

In the interest of expediting the allowance of present application, claim 46 has been amended to exclude compounds represented by the general formula X, wherein one of the substituents on nitrogen is acyl containing alkyl group, by striking CR<sub>7</sub>R<sub>8</sub> from list of "Z" substituents. Compounds of the claimed invention represented by the general chemical formula Y differ from cationic lipids disclosed by Nantz by having a *carboxy*, rather than *acyloxy*, containing alkyl group. Presence of the terminal carboxyl group is advantageous, in that due to its chemical reactivity it can be further derivatized with amino acid, peptide, polypeptide, protein, nucleic acid, etc. (See [0296] of the published application). The Nantz patent does not teach or suggest, explicitly or implicitly, a compound having a functional group corresponding to COOR'' in claims 64, 67, 69-70, and 83-84.

The Office contends that Felgner teaches that positively charged synthetic cationic lipids are capable of facilitating intracellular delivery of biologically active substances. The Office further states that it would have been *prima facie* obvious "to

employ the cationic lipid compounds as disclosed by Nantz *et al.* ... to form a lipid-DNA complex with a net positive charge to elicit the predictable result...". Applicant respectfully reiterates that the cationic lipid compounds disclosed in the present invention differ from the compounds taught by Nantz *et al.* by the presence of a carboxyl group. Because the Nantz patent does not teach or suggest, explicitly or implicitly, a compound having a functional group corresponding to COOR" in instant claims, the Office 's argument that the employment of the lipids taught by Nantz to form a lipid-DNA complex for transfection into a cell renders present invention obvious is moot.

For at least these reasons, the Nantz patent and the Felgner publication do not render claims 64, 67, 69-70, and 83-84 *prima facie* obvious. Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

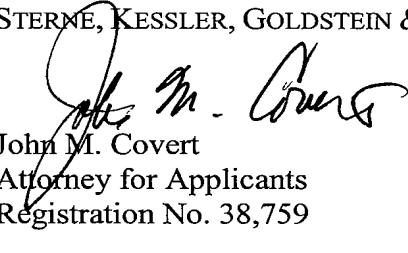
***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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